Integrative Approaches to Dyslipidemia

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Objectives

- To be able to recommend a diet that will nourish your patients and help with dyslipidemia.
- To discuss Integrative strategies to help with dyslipidemia.
- To learn alternative treatments for patients who are intolerant to statins.

About the speaker:

- Board certified in Emergency Medicine
- Board certified in Integrative Medicine
- Works in the local emergency rooms
- Owner of PflegMed: Center for Integrative Medicine
- Wife and mother of four



What is dyslipidemia?

- Dyslipidemia is an abnormal amount of lipids (e.g. triglycerides, cholesterol and/or fat phospholipids) in the blood.
- Hyperlipidemia is the elevation of lipids in the blood
- Causes
 - Genetic
 - Secondary causes: diet, lifestyle, metabolic disease, hormones, medication, liver diseases, renal diseases

Why we need cholesterol?

- Lipoproteins transport lipids (hydrophobic fat molecules) to target tissues. The major circulating lipids transported thus include:
- Cholesterol: essential for cell membranes; substrate for steroid hormones and bile acids
- Cholesterol esters: most cholesterol in plasma is in this form
- Triglycerides: three carbon glycerol backbone linked to three fatty acids; hydrolysis of triglycerides generates free fatty acids needed for energy
- Phospholipids: essential for cell membranes; participate in signal transduction pathways; generate free fatty acids such as arachidonate

LDL

- Elevated LDL-C a pathogenic factor for atherosclerosis
- LDL-C is produced in different sizes
- Small, dense LDL-C is more easily oxidized making it more atherogenic
- Factors that predispose to high LDL levels?
- Metabolic syndrome, diabetes, eating a high glycemic diet, a sedentary lifestyle and obesity.



- Optimal level >60
- How to increase?
- Causes for low HDL:
 - Low fat diets
 - Cigarette smoking

Causes of Low HDL-C and High HDL-C

• Adapted from: Ballantyne, Christie M. 2009. Clinical Lipidology: A Companion to Braunwald's Heart Disease. Saunders, an imprint of Elsevier Inc.

	Low HDL-C	High HDL-C
General	Acute illness	
	Cigarette smoking Very-low-fat diet	Aerobic activity Alcohol consumption
Genetic	ABCA apoA LCAT	CETP Hepatic lipase Endothelial lipase
	Visceral obesity Insulin resistance Diabetes mellitus	
Inborn errors of metabolism	Gaucher disease Glycogen storage disease Niemann-Pick disease	
	Anabolic steroids B-blockers Probucol	Estrogenic compounds Corticosteroids Antiseizure medications B2-agonists Niacin Fibrates
Miscellaneous	Celiac sprue Lymphoma	Paraproteinemia

ABCA1, ATP-binding cassette transporter A1; apoA-I, apolipoprotein A-I; CETP, cholesteryl ester transfer protein; HDL, high-density lipoprotein; LCAT, lecithin: cholesterol acyltransferase.

Triglycerides (TG)

- Major causes of elevated TGs
 - Obesity
 - Cigarette smoking
 - High carbohydrate diet
 - Excessive alcohol intake
- Other diseases- insulin resistance and diabetes, hypothyroidism, nephrotic syndrome, chronic kidney disease, obstructive sleep apnea, PCOS, HIV, Cushing's syndrome, anorexia, paraproteinemia, acute intermittent porphyria

Lipoprotein (a)

- High levels risk for CVD and stroke
- Defined by diet more less by diet/lifestyle compared with other fats
- Still, lower other risk factors (diet, nutrition, lifestyle) while medications are being studied
- Can get a genetic test (chromosome 19 APEO SNPs)- accesses genetic risk of CAD, DM2, stroke, increased LDL.

Hormone cascade

Hormone cascade start with cholesterol

- Building block of all steroid hormones
- Healthy fats and cholesterol are needed to make hormones

Nutrition for Dyslipidemia

- Low-fat, low-cholesterol diet
- NO!!
- Low-fat foods usually have more carbs
- Eating low-fat can be difficult, focus on the good fats

Using Food as Medicine: Green Tea

- Green Tea (Camellia sinensis)
- Reduction in total and LDL cholesterol levels
- No significant effect on HDL cholesterol or triglyceride levels.
- 5-8 cups of organic green tea would be optimal for lipid improvement but probably not reasonable
- Other health benefits with drinking green tea

Kim A, Chiu A, Barone MK, Avino D, Wang F, Coleman CI, Phung OJ. Green tea catechins decrease total and low-density lipoprotein cholesterol: a systematic review and meta-analysis. J Am Diet Assoc. 2011 Nov;111(11):1720-9. doi: 10.1016/j.jada.2011.08.009. PMID: 22027055.

Using Food as Medicine: Nuts

- High in monounsaturated fats
- Subjects consuming 5 or more times a week had a 20% lower risk of CHD and 14% lower risk of CVD when compared to those that ate little or no nuts
- Improvement of lipid profile
- Note- it is a high calorie food and patients should be advised: serving size is 1 oz.

Guasch-Ferré M, Liu X, Malik VS, Sun Q, Willett WC, Manson JE, Rexrode KM, Li Y, Hu FB, Bhupathiraju SN. Nut Consumption and Risk of Cardiovascular Disease. J Am Coll Cardiol. 2017 Nov 14;70(20):2519-2532. doi: 10.1016/j.jacc.2017.09.035. PMID: 29145952; PMCID: PMC5762129.

O'Neil CE, Keast DR, Nicklas TA, Fulgoni VL 3rd. Nut consumption is associated with decreased health risk factors for cardiovascular disease and metabolic syndrome in U.S. adults: NHANES 1999-2004. J Am Coll Nutr. 2011 Dec;30(6):502-10. doi: 10.1080/07315724.2011.10719996. PMID: 22331685.

Using Food as Medicine: Garlic

- Garlic (Allium sativum)
- 1 4 cloves per day or 600 900 mg dried garlic
- If used for at least two months: Redection in total serum cholesterol by 17 ± 6 mg/dL and low-density lipoprotein cholesterol by 9 ± 6 mg/dL in individuals with elevated total cholesterol levels (>200 mg/dL)

Ried K, Toben C, Fakler P. Effect of garlic on serum lipids: an updated meta-analysis. Nutr Rev. 2013 May;71(5):282-99. doi: 10.1111/nure.12012. Epub 2013 Mar 7. PMID: 23590705.

GOOD	Monounsaturated Fat -olives, olive and canola oils, most nuts, and avocados	Lowers LDL	Raises HDL	
GOOD	Polyunsaturated Fat -fish high in omega-3, soybean and safflower	Lowers LDL	Raises HDL	
OK	Saturated Fat red meat, dairy products, butter, coconut	Raises LDL	Raises HDL	
UGLY	Trans Fat margarine; vegetable shortening, partially hydrogenated oil	Raises LDL	Lowers HDL	Raises TG

And I must mention PUFAs

- polyunsaturated fats can be more unstable when heating
- due to their chemical structure. That being said they are more likely to oxidize when heated
- A study was done studying endothelial (blood vessel) function after eating meals with commercial fried food (PUFAs oil). It showed impaired endothelial function, most likely from the lipid oxidation. Contrast this to a study done where walnuts and olive oil was added to a meal where it protected endothelial vessels.
- There have even been independent studies which show a concern that PUFAs (which are high in linoleic acid- I will talk about this more in my stories or another post) can impair our cell membranes for up to 140 days.... Let that sink in. □ So it's not fat but the type of fat we are consuming which is causing the issues.
- https://pubmed.ncbi.nlm.nih.gov/17045905/. and https://pubmed.ncbi.nlm.nih.gov/10091835/

Good fats vs Bad fats

A guide to FATS: What to eat and what to avoid



Soybean oil Canola oil Sunflower oil Grapeseed oil Sunflower oil Cottonseed oil Safflower oil Corn oil Expeller pressed

@integrativedrmom

What diet to recommend?

- It should be personalized and thought more of a lifestyle then a diet.
- Mediterranean diet is well studied
 - Increased HDL with significant decrease in LDL
 - Decreased triglycerides (up to 13 mg/dl)
 - Decreased SBP (6.5 mm Hg) and DBP (2.1 mm Hg)

Ndanuko RN, Tapsell LC, Charlton KE, Neale EP, Batterham MJ. Dietary Patterns and Blood Pressure in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2016 Jan 15;7(1):76-89. doi: 10.3945/an.115.009753. PMID: 26773016; PMCID: PMC4717885.

Walnuts



Walnuts

- Lowers LDL-C
- Raises HDL-C
- Lowers TG
- This is an ideal heart-healthy food.
- Substituting walnuts for part of the mono-unsaturated fat in a cholesterol-lowering Mediterranean diet further reduced total and LDL cholesterol levels in men and women with hypercholesterolemia.

Zambón D, Sabaté J, Muñoz S, Campero B, Casals E, Merlos M, Laguna JC, Ros E. Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women. A randomized crossover trial. Ann Intern Med. 2000 Apr 4;132(7):538-46. doi: 10.7326/0003-4819-132-7-200004040-00005. Erratum in: Ann Intern Med 2000 Oct 17;133(8):659. PMID: 10744590.

Animal fats



Animal fats

- Mixed results in the studies
- Raises LDL-C
- Raises HDL-C
- Keto diet? Insulin sensitivity play a role?

Low fat cookies



Low fat cookies

- Raises LDL-C
- Raises TG
- Bad Cookie! Not only does this raise LDL cholesterol, but also increases Triglycerides. This doesn't even address the bad carbs and affects on blood sugar. Avoid this type of food.

Butter vs. Margarine vs. Olive oil



Margarine

- Lowers HDL-C
- Raises LDL-C
- Raises TG
- Stay away from this! This is the trifecta of negative affects on lipids. Raises both LDL-C and TG while decreasing your HDL-C.

Butter

- Raises LDL-C
- Raises TG
- Raises HDL-C
- Eat in moderation. LDL cholesterol increases with higher amounts of Saturated Fat from whole milk and butter in the diet (when substituted for carbs or unsaturated fatty acids). But this increase in saturated fats may also increase HDL and therefore might not affect or even lower the total cholesterol:HDL cholesterol ratio

Huth PJ, Park KM. Influence of dairy product and milk fat consumption on cardiovascular disease risk: a review of the evidence. Adv Nutr. 2012 May 1;3(3):266-85. doi: 10.3945/an.112.002030. PMID: 22585901; PMCID: PMC3649459.

Olive oil

- Raises HDL-C
- Lowers LDL-C
- Heart-healthy! Mediterranean diet staple!
- Make sure you store in dark cupboard, not next to heat, get a high quality extra virgin olive oil

Avocados



Avocados

- Raises HDL-C
- Lowers LDL-C
- Lowers TG
- A great monounsaturated fat!
- Look for dressing with avocado oil in them instead of toxic oils





Salmon

- Lowers LDL-C
- Raises HDL-C
- Great source of omega-3 fatty acids EPA and DHA
- Make sure to get wild caught, farmed salmon can actually contain more omega-6

Lifestyle Interventions: Exercise

- Exercise 30 minutes a day, beneficial for lipid profile
- Increase in LDL particle size and a reduction in small LDL particles



Kraus WE, Houmard JA, Duscha BD, Knetzger KJ, Wharton MB, McCartney JS, Bales CW, Henes S, Samsa GP, Otvos JD, Kulkarni KR, Slentz CA. Effects of the amount and intensity of exercise on plasma lipoproteins. N Engl J Med. 2002 Nov 7;347(19):1483-92. doi: 10.1056/NEJMoa020194. PMID: 12421890.

Lifestyle Interventions: Yoga

- Favorable effects on HDL cholesterol and triglycerides
- Helpful also with HTN



Hartley L, Dyakova M, Holmes J, Clarke A, Lee MS, Ernst E, Rees K. Yoga for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2014 May 13;(5):CD010072. doi: 10.1002/14651858.CD010072.pub2. PMID: 24825181.

Traditional Treatments

- Statins -HMG CoA reductase inhibitors
- Bile acid Sequestrants
- Ezetimibe (Zetia) -cholesterol absorption inhibitor
- Fibrates



Statins

- lipid-soluble statins (simvastatin, lovastatin, atorvastatin)
- water-soluble statin (pravastatin, rosuvastatin and Fluvastatin)

Derived from fungi	Synthetic
lovastatin (Mevacor)	fluvastatin (Lescol)
simvastatin (Zocor)	atorvastatin (Lipitor)
pravastatin (Pravachol)	rosuvastatin (Crestor)
	pitavastatin (Livalo)

Statins MOA

- Statin drugs block the enzyme HMG-CoA (3-hydroxy-3methyglutaryl CoA) reductase
- This inhibits the liver's ability to produce LDL

What about once a week dosing?

- the HD-ROWS study
- rosuvastatin 80 mg once weekly (n = 10) or atorvastatin 10 mg daily (n = 10), for 8 weeks.
- "Rosuvastatin 80 mg once weekly produced comparable lipid changes to atorvastatin 10 mg daily when measured at specific points after the last dose. Our findings support previous data demonstrating a significant reduction in LDL-C with once weekly statin dosing."

Backes JM, Gibson CA, Ruisinger JF, Moriarty PM. The high-dose rosuvastatin once weekly study (the HD-ROWS). J Clin Lipidol. 2012;6(4):362-367. doi:10.1016/j.jacl.2011.11.002

Statins

- Water soluble and once a week dosing an option?
- Side effects- switch statin therapy
- *clinical pearl- always supplement with CoQ10 when patient is on a statin ((ubiquinol is absorbed better than ubiquinone))
- Statins deplete CoQ10



Rakel: Textbook of Integrative Medicine

Red Yeast Rice

- A fermented product of rice
- Contains monocolins which inhibit cholesterol synthesis through HMG-CoA
- Been shown to lower elevated low-density lipoprotein (LDL) cholesterol by approximately 20%
- Also contains amino acids, flavonoids, trace elements, sterols, isoflavones and monounsaturated fats
- Recommended dose 800 4800 md per day of standardized RYR
- Do not use with statins

Studies on RYR

- Patients give RYR who could not tolerate statins
- RYR 1800 mg BID or placebo
- "Levels of HDL cholesterol, triglyceride, liver enzyme, or CPK; weight loss; and pain severity scores did not significantly differ between groups at either week 12 or week 24"
- Becker DJ, Gordon RY, Halbert SC, French B, Morris PB, Rader DJ. Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial. Annals of Internal Medicine 150(12):830-9, W147-9. Jun, 2009.

RYR studies

- Red yeast rice 2,400 mg twice daily or pravastatin 20 mg twice daily for 12 weeks
- "The low-density lipoprotein cholesterol level decreased 30% in the red yeast rice group and 27% in the pravastatin group."
- Halbert SC, French B, Gordon RY, et al. Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. *Am J Cardiol*. 2010;105(2):198-204. doi:10.1016/j.amjcard.2009.08.672

Fun fact

- Lovastatin, the progenitor of the statin family, is in fact a naturally occurring compound produced by the yeast Monascus purpureus
- RYR contains monacolin K, which is lovastatin, and eight other monacolins, along with sterols, isoflavones, and monounsaturated fatty acids.

Niacin (B3)

 Increases HDL-C by 20% and decreases LDL-C, triglycerides and lipoprotein (a)

Gordon SM, Amar MJ, Jeiran K, et al. Effect of niacin monotherapy on high density lipoprotein composition and function. *Lipids Health Dis.* 2020;19(1):190. Published 2020 Aug 21. doi:10.1186/s12944-020-01350-3

Niacin (B3)

- Dosing ranges from 500 4000 mg/day
- Sustained release is best. (nonflushing niacin not improve lipid panels)
- Flushing side effects can be minimized by titrating dose, taking with meals, consumption with baby asa and supplemental quercetin (500 mg)
- **Contraindications:** Active liver disease or unexplained LFT elevations, Peptic ulcer disease

Berberine (Berberis vulgaris)

- Lowers LDL by increased hepatic expression of LDL receptors
- Also, activates adenosine monophosphate-activated kinase (AMPK), similar to metformin, lowers triglycerides, improves metabolic syndrome
- Dosing: 500 mg BID

Contraindicated with cyclosporine

McCarty MF, O'Keefe JH, DiNicolantonio JJ. Red Yeast Rice Plus Berberine: Practical Strategy for Promoting Vascular and Metabolic Health. *Altern Ther Health Med.* 2015;21 Suppl 2:40-45.

Bergamot (Citrus bergamia)

- Contains high amount of flavonoids
- Reduces total cholesterol, LDL and triglycerides
- Phytochemicals in bergamot maybe prevent and lower LDL particle oxidation
- Has a role in energy metabolism and glucose metabolism
- 500 mg BID

Nauman MC, Johnson JJ. Clinical application of bergamot (*Citrus bergamia*) for reducing high cholesterol and cardiovascular disease markers. Integr Food Nutr Metab. 2019 Mar;6(2):10.15761/IFNM.1000249. doi: 10.15761/IFNM.1000249. Epub 2019 Feb 28. PMID: 31057945; PMCID: Perna S, Spadaccini D, Botteri L, Girometta C, Riva A, Allegrini P, Petrangolini G, Infantino V, Rondanelli M. Efficacy of bergamot: From anti-inflammatory and anti-oxidative mechanisms to clinical applications as preventive agent for cardiovascular morbidity, skin diseases, and mood alterations. Food Sci Nutr. 2019 Jan 25;7(2):369-384. doi: 10.1002/fsn3.903. PMID: 30847114; PMCID: PMC6392855.

Plant Sterols- Phytosterols

- Dose-dependent reduction on serum lipids
- They reduce cholesterol absorption from the gut
- B-sitosterol, campesterol, stigmasterol
- Ex: a dose of 1.6 2 grams per day (divided over two meals) may reduce LDL-C by 9-205
- No effect on HDL or triglyercides
- Effect on LDL is additive, can be combined with statins

Plant Sterols- Phytosterols

- Food examples high in plant sterols:
- Nuts- almonds, walnuts, cashews, pecans, pistachios
- Flaxseed
- Broccoli
- Carrots
- Brussel sprouts
- Lettuce

In summary

- Always meet your patient where they are at- not every diet, medication or supplement will work for everyone
- What works best for your practice? Customize for your practice. Make a handout with your personal recommendations based on your knowledge and experience.
- If recommending supplements, make sure they are using high quality supplements.
- You are an amazing advocate for your patient, taking the time to learn on a Sunday is dedication- keep up the great work!

Thank you! Questions?



Where to find me!

- E-mail <u>drjen@pflegmed.com</u>
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Additional References

- McCarty MF, O'Keefe JH, DiNicolantonio JJ. Red Yeast Rice Plus Berberine: Practical Strategy for Promoting Vascular and Metabolic Health. *Altern Ther Health Med.* 2015;21 Suppl 2:40-45.
- Yadav R, Liu Y, Kwok S, et al. Effect of Extended-Release Niacin on High-Density Lipoprotein (HDL) Functionality, Lipoprotein Metabolism, and Mediators of Vascular Inflammation in Statin-Treated Patients. *J Am Heart Assoc*. 2015;4(9):e001508. Published 2015 Sep 15. doi:10.1161/JAHA.114.001508
- Integrative Medicine E-Book 4th Edition, by <u>David Rakel</u>